

THE CLAIMS

What is claimed is:

1. A freeze dried biocompatible porous matrix useful as a scaffold for growing cells, the matrix including plasma proteins comprising fibrinogen, thrombin and Factor XIII, and at least one anti fibrinolytic agent, wherein at least 50% by weight of the total protein content is fibrin, and the matrix has substantially uniform pores, is substantially devoid of organic chelating agents and has a residual moisture below 3%.
2. The matrix according to claim 1 wherein the plasma proteins are present with at least 0.5 units of thrombin per mg protein.
3. The matrix according to claim 1 wherein at least one of the plasma proteins is autologous.
4. The matrix according to claim 1 wherein all the plasma proteins are autologous.
5. The matrix according to claim 1 wherein the anti-fibrinolytic agent is tranexamic acid present in an amount of at least 5%.
6. The matrix according to claim 1 further comprising at least one auxiliary component selected from the group consisting of polysaccharides, anionic polysaccharides, glycosaminoglycans, or synthetic polymers.
7. The matrix according to claim 6 wherein the auxiliary component is selected from a group consisting of hyaluronic acid, pectin, alginate, galactans, galactomannans, glucomannans, polyuronic acids, heparin, chondroitin sulfate, dextran sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, hexuronyl hexosaminoglycan sulfate, inositol hexasulfate, sucrose octasulfate and PEG.
8. The matrix according to claim 7 wherein the wherein the auxiliary component is dextran sulfate or hyaluronic acid.

9. The matrix according to claim 1 wherein the cells are stem cells or progenitor cells.

10. The matrix according to claim 1 wherein the cells are selected from the group consisting of chondrocytes, osteocytes, hepatocytes, mesenchymal, epithelial, urothelial, neuronal, pancreatic, renal and ocular cell types.

11. The matrix according to claim 1 wherein the cells attain a density of at least 10^4 cells per cm^3 .

12. The matrix according to claim 1 further comprising at least one bioactive agent, selected from the group consisting of growth factors, cytokines, enzymes, anti-microbials, and anti inflammatory agents.

13. The matrix according to claim 1 having pores in the size range of 50-300 microns.

14. A method for preparing a porous matrix of plasma proteins useful as a scaffold for growing cells in vitro, the method comprising the steps of: mixing plasma proteins with thrombin in the presence of calcium ions and at least one anti-fibrinolytic agent under conditions suitable for clotting and in the substantial absence of organic chelating agents, optionally with adding of at least one auxiliary component thereto; casting the mixture of plasma proteins, thrombin, anti-fibrinolytic agent and optional auxiliary agent upon a solid support prior to clotting; freezing the clotted mixture; and lyophilizing the clotted mixture to obtain a sponge having no more than 3% residual moisture.

15. The method according to claim 14 wherein the plasma proteins comprise at least fibrinogen and factor XIII.

16. The method according to claim 14 wherein at least one of the plasma proteins is autologous.

17. The method according to claim 14 wherein all the plasma proteins are autologous.

18. The method according to claim 14 wherein the plasma proteins are mixed with at least 0.5 units of thrombin per mg protein.

19. The method according to claim 14 wherein the anti-fibrinolytic agent comprises tranexamic acid in an amount of at least 5%.

20. The method according to claim 14 wherein the at least one auxiliary component is present and is selected from the group consisting of polysaccharides, anionic polysaccharides, glycosaminoglycans, and synthetic polymers.

21. The method according to claim 14 wherein the at least one auxiliary component is present and is selected from the group consisting of hyaluronic acid, pectin, alginate, galactans, galactomannans, glucomannans, polyuronic acids, heparin, chondroitin sulfate, dextran sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, hexuronyl hexosaminoglycan sulfate, inositol hexasulfate, sucrose octasulfate and PEG.

22. The method according to claim 20 wherein the auxiliary component is present and is dextran sulfate or hyaluronic acid.

23. A method for preparing a porous scaffold useful for implantation *in vivo*, comprising the steps of: mixing plasma proteins with thrombin in the presence of calcium ions and at least one anti-fibrinolytic agent under conditions suitable for clotting, and in the substantial absence of organic chelating agents, optionally with adding of at least one auxiliary component; casting the mixture of plasma proteins, thrombin, anti-fibrinolytic agent and optional auxiliary component upon a solid support prior to clotting; freezing the clotted mixture; lyophilizing the clotted mixture to obtain a sponge; cutting the sponge into sections of desired shape; seeding the sections with cells; growing the cells on the sections until the cells reach a density of at least 10^4 cells per cm^3 ; and implanting the seeded sections *in vivo*.

24. The method according to claim 23 wherein the plasma proteins comprise at least fibrinogen and factor XIII.

25. The method according to claim 23 wherein at least one of the plasma proteins is autologous.

26. The method according to claim 23 wherein all the plasma proteins are autologous.
27. The method according to claim 23 wherein the plasma proteins are mixed with at least 0.5 units of thrombin per mg protein.
28. The method according to claim 23 wherein the anti-fibrinolytic agent comprises tranexamic acid in an amount of at least 5%.
29. The method according to claim 23 wherein the at least one auxiliary component is present and is selected from the group consisting of polysaccharides, anionic polysaccharides, glycosaminoglycans, and synthetic polymers.
30. The method according to claim 23 wherein the auxiliary component is present and is selected from the group consisting of hyaluronic acid, pectin, alginate, galactans, galactomannans, glucomannans, polyuronic acids, heparin, chondroitin sulfate, dextran sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, hexuronyl hexosaminoglycan sulfate, inositol hexasulfate, sucrose octasulfate and PEG.
31. The method according to claim 23 wherein the auxiliary component is present and is dextran sulfate or hyaluronic acid.
32. The method according to claim 23 wherein the at least one auxiliary component is present and is a bioactive agent selected from the group consisting of growth factors, cytokines, enzymes, anti microbials, and anti-inflammatory agents.
33. The method according to claim 23 wherein the cells are selected from the group consisting of chondrocytes, hepatocytes, osteocytes, mesenchymal, epithelial, urothelial, neuronal, pancreatic, renal and ocular cell types.
34. A method for preparing a porous scaffold useful for support of cell growth after implantation *in situ*, comprising the steps of: mixing plasma proteins with thrombin in the presence of calcium ions and at least one anti-fibrinolytic agent under conditions suitable for clotting, and in the substantial absence of organic chelating agents, optionally with adding

of at least one auxiliary component; casting the mixture of plasma proteins, thrombin anti-fibrinolytic agent and optional auxiliary component upon a solid support prior to clotting; freezing the clotted mixture; lyophilizing the clotted mixture to obtain a sponge having no more than 3% residual moisture; optionally washing the sponge to remove soluble auxiliary components; optionally re-lyophilizing the washed sponge to reduce residual moisture to no more than 3%; cutting the sponge into sections of desired shape; and implanting the sections *in situ*.

35. The method according to claim 34 wherein the plasma proteins comprise at least fibrinogen and factor XIII.

36. The method according to claim 34 wherein at least one of the plasma proteins is autologous.

37. The method according to claim 34 wherein all the plasma proteins are autologous.

38. The method according to claim 34 wherein the plasma proteins are mixed with at least 0.5 units of thrombin per mg protein

39. The method according to claim 34 wherein the anti-fibrinolytic agent comprises tranexamic acid in an amount of at least 5%.

40. The method according to claim 34 wherein the at least one auxiliary component is present and is selected from the group consisting of polysaccharides, anionic polysaccharides, glycosaminoglycans, or synthetic polymers.

41. The method according to claim 34 wherein the at least one auxiliary component is present and is selected from the group consisting of hyaluronic acid, pectin, alginate, galactans, galactomannans, glucomannans, polyuronic acids, heparin, chondroitin sulfate, dextran sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, hexuronyl hexosaminoglycan sulfate, inositol hexasulfate, sucrose octasulfate and PEG.

42. The method according to claim 34 wherein the at least one auxiliary component is present and is dextran sulfate or hyaluronic acid.
43. The method according to claim 34 wherein the at least one auxiliary component is present and is a bioactive agent selected from the group consisting of growth factors, cytokines, enzymes, anti microbials, and anti-inflammatory agents.
44. The method according to claim 34 wherein the cells are selected from the group consisting of chondrocytes, osteocytes, hepatocytes, epithelial, urothelial, neuronal, mesenchymal, pancreatic, renal and ocular cell types.
45. The method according to claim 34 which further comprises seeding the sections with cells and growing the cells on the sections until the cells reach a density of at least 104 cells per cm³.
46. The method according to claim 34 which further comprises seeding the sections with cells *in vivo* at a site of treatment.
47. An implant prepared according to claim 14.
48. A method for treating injured tissue, the method comprising the step of implanting into an injury site an implant according to claim 47.
49. The method according to claim 48 wherein the injured tissue to be treated is skeletal tissue.
50. A porous coating for an implant comprising the matrix according to claim 1.